

REMARKS/ARGUMENTS

Claims 1-26 are pending in the application. Claims 1-9 and 13-25 are canceled without prejudice to subsequent revival. Applicants reserve the right to prosecute claims 1-9 and 13-25 in a divisional application.

Claims 10-12 and 26 are under examination. No claims are allowed. Claim 26 has been canceled. Claims 10-12 have been amended. Entry of the amendment, reconsideration of the rejection, and allowance of claims 10-12 are requested.

The Amendment

In order to expedite prosecution of the application and advance the case toward allowance, the claims have been amended. No new matter was added by the amendment.

The specification and abstract have been amended to provide for proper use of the trademark "PRONASE" protease. The word "pronase" has been replaced with "PRONASE protease" throughout the specification, according to the Examiner's suggestion.

Claim 10 has been amended to clarify that SGT is "Streptomyces griseus trypsin (SGT)" as requested by the Examiner. Claim 10 has also been amended to clarify that the preparation has "a purity of at least 95% and further comprises arginine". Support for this amendment can be found in the specification on page 10, paragraph [034], lines 5-7 and paragraph [035], lines 1-8; and on page 9, paragraph [030].

Claim 11 has been amended to delete the phrase "and having a purity of at least 95%" because claim 11 depends on amended claim 10 which includes that phrase.

Claim 12 has been amended to replace the word "said pronase" with "PRONASE protease" as requested by the Examiner. Claim 12 has also been amended to delete the dependency on claim 10. Instead, claim 12 now specifies that the preparation is "a purified preparation of Streptomyces griseus trypsin (SGT) having a specific activity of at least about 25 x 10³ U/mg protein and a purity of at least 95%". Support for this amendment can be found on page 10, paragraph [035], lines 6-8 and page 11, paragraph [037], line 4.

Claim 26 has been canceled.

Specification

The Office Action states the trademark PRONASE must be capitalized wherever it appears and be accompanied by the generic terminology. Thus, Applicants have amended the specification to refer to "PRONASE protease".

Claim Objections

Claims 10 and 26 have been objected to for using the term SGT without first identifying the acronym. Applicants have amended claim 10 to clarify that SGT is "Streptomyces griseus trypsin (SGT)" as requested by the Examiner. Claim 26 has been canceled.

Claim 12 has been objected to for using the tradename PRONASE without writing the word in uppercase letters. Hence, Applicants have amended claim 12 to replace the word "said pronase" with "PRONASE protease".

Rejections under 35 U.S.C. §102

Claims 10 and 12 are rejected under 35 U.S.C. §102(b) as being anticipated by Koo *et al.* for teaching the purification of SGT from PRONASE protease with a result yield of 62672 and 31155 U/mg which allegedly meets the claim limitations. The Examiner indicates that the reference does not disclose the purity of the trypsin preparation.

To the extent that the rejection applies to the claims as amended, Applicants respectfully traverse the rejection.

"In order for a rejection under §102(b) to be valid, each and every element of the claim must be found in the prior art reference." (MPEP 2131; *In re Royka and Martin*, 180 USPQ 580 (CCPA 1974)).

Claim 10 has been amended to specify that the SGT preparation has a purity of at least 95% and further comprises arginine. As indicated in the Office Action, Koo *et al.* do not disclose the purity of the trypsin preparation. However, Koo *et al.* disclose that purification of SGT from PRONASE protease is carried out by several chromatography steps and the protein is eluted with a stepwise gradient of 50 mM to 500 mM KCl in Buffer A (see Koo *et al.*, page 335,

throughout column 2) or with 10 mM Tris-Cl (see Koo *et al.*, page 335, end of column 2). In comparison, the instant invention is directed to isolated SGT, prepared by a single chromatography step (see page 5 of the specification, paragraph [021], line 2), using an amidine, a guanidine, or an amine containing species, preferably arginine, as an eluant (see page 6, paragraphs [022] and [023]; and page 9, paragraphs [030] and [031]). Thus, the SGT composition of the instant invention comprises arginine in its final preparation. Koo *et al.* do not disclose or suggest a composition with arginine in its final preparation and can therefore not anticipate claim 10.

Claim 12 is a product by process claim that has been amended to include purity. As such the purified preparation of *Streptomyces griseus* trypsin (SGT) is specified to have a purity of at least 95%. According to the Examiner, patentability of product by process claims is based upon the product itself and not the process used to make it. Since Koo *et al.* do not disclose the purity of the trypsin preparation the reference cannot anticipate claim 12.

In light of the above amendment and remarks, Applicants respectfully request that the rejection of claims 10 and 12 under 35 U.S.C. §102(b) be withdrawn.

Claim 26 is rejected under 35 U.S.C. §102(b) as being anticipated by Kasai. The Office Action indicates that this claim allegedly reads on purified preparations of trypsin of at least 95% purity.

Claim 26 has been canceled, hence, this rejection is moot.

Rejections under 35 U.S.C. §103

Claim 11 is rejected under 35 U.S.C. §103(a) as being unpatentable over Koo *et al.* in view of Kasai. The Examiner indicates that Koo *et al.* disclose an SGT preparation with the claimed specific activity but do not disclose the purity level of the preparation. The Examiner further asserts that it would have been obvious to one of ordinary skill in the art to improve the purity level of that preparation by further purifying it using the method of Kasai.

"The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure." *In re*

Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). "Obviousness is measured by considering whether a hypothetical person having all the art at hand would have found the same solution when addressing himself to the same problem." (*Stratoflex Inc. v. Aeroquip Corporation*, 561 F.Supp. 618, 218 USPQ 231, 239 (Mich. 1982).

Claim 11 is directed to a purified preparation of SGT comprising arginine at a concentration of at least about 0.5 M. As shown above, Applicants use a method of isolating SGT via a single chromatography step, using preferably arginine as an eluant, wherein the SGT composition comprises arginine in its final preparation.

In comparison, Kasai (like Koo *et al.*) employs an entirely different solution to elute active trypsin and produces a different preparation. In fact, neither Kasai nor Koo *et al.* teach a purified preparation of SGT that includes arginine. Kasai observed that "only a more acidic eluant such as 5 mM HCl could elute the active trypsin" (see page 5, column 2, paragraph 2, line 9), thus, resulting in a higher purity. At a lower pH (7.2-4.0) adsorption, instead of retardation of active trypsin occurred which could not be remedied by washing with 20 column volumes of buffer (see page 5, column 2, paragraph 2, lines 4-7). Kasai then uses benzamidine to elute adsorbed trypsin (see page 5, column 2, paragraph 3, section (3)). As such, Kasai's solution to the problem of isolating active trypsin is clearly outside Applicants' teachings. Notably, Kasai's disclosure distinctly indicates that eluting active trypsin at lower pH levels was not successful (*supra*) which is exactly opposite to Applicants' teachings. Thus, neither the combination of the references by Koo *et al.* and Kasai nor Kasai alone suggest the limitations of claim 11.

In light of the above amendment and remarks, Applicants respectfully request that the rejection of claim 11 under 35 U.S.C. §103(a) be withdrawn.

Appl. No. 10/006,223
Amdt. dated September 16, 2003
Reply to Office Action of June 17, 2003

PATENT

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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